## CLAIMS

- A method of treating or preventing an infection in a subject who has been
   exposed to or is at risk for exposure to Bacillus anthracis, Yersinia pestis, Variola major, Histoplasma capsulatum, Haemophilus influenzae, Escherichia coli, Shigella flexneri, S. dysenteriae (Shigella bacillus), Salmonella, Staphylococcus enterotoxin B, Ebola virus, tick-borne encephalitis virus, botulinum toxin, ricin toxin, cobra venom, shellfish toxin, botulinum toxin, saxitoxin, ricin toxin, tricothecene
   mycotoxin, or aflatoxin, comprising administering to the subject a therapeutically effective amount of an immunostimulatory D oligodeoxynucleotide or an immunostimulatory K oligodeoxynucleotide, thereby treating or preventing the infection.
- 2. The method of claim 1, wherein the subject has been exposed to or is at risk for exposure to *Bacillus anthracis*.
  - 3. The method of claim 1, wherein the subject has been exposed to or is at risk for exposure to Ebola virus.

- 4. The method of claim 1, wherein the subject has been exposed to or is at risk for exposure to tick-borne encephalitis virus.
- 5. The method of claim 1, wherein the infection is anthrax, smallpox, Ebola, or tick-borne encephalitis.
  - 6. The method of claim 5, wherein the infection is anthrax.
- 7. The method of claim 1, wherein the oligodeoxynucleotide is at least about
   30 16 nucleotides in length and comprises a sequence represented by the following formula:

wherein the central CpG motif is unmethylated, Pu is a purine nucleotide, Py is a pyrimidine nucleotide, X and W are any nucleotide, M is any integer from 0 to 10, and N is any integer from 4 to 10.

- 5 8. The method of claim 7, wherein N is about 6.
  - 9. The method of claim 7, wherein Pu<sub>1</sub> Py<sub>2</sub> CpG Pu<sub>3</sub> Py<sub>4</sub> are phosphodiester bases.
- 10. The method of claim 7, wherein X<sub>4</sub>X<sub>5</sub>X<sub>6</sub>(W)<sub>M</sub> (G)<sub>N</sub> comprises one or more phosphothioate bases.
  - 11. The method of claim 7, wherein  $X_1X_2X_3$  Pu Py and Pu Py  $X_4X_5X_6$  are self complementary.

15

20

- 12. The method of claim 1, wherein the oligodeoxynucleotide comprises a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, and SEQ ID NO: 25.
- 13. The method of claim 1, wherein the oligodeoxynucleotide comprises a sequence represented by the following formula:

25

wherein the central CpG motif is unmethylated, Q is T, G or A, W is A or T, and  $N_1$ ,  $N_2$ ,  $N_3$ ,  $N_4$ ,  $N_5$ , and  $N_6$  are any nucleotides.

14. The method of claim 13, wherein Q is a T.

- 15. The method of claim 1, wherein the oligodeoxynucleotide comprises a sequence selected from the group consisting of SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, and SEQ ID NO: 43.
- 16. The method of claim 1, wherein the oligodeoxynucleotide is administered intravenously, intra-muscularly, subcutaneously, or by inhalation.
- 17. The method of claim 1, wherein the oligodeoxynucleotide is administered intra-muscularly.
- 18. A method of treating or preventing an infection in a subject who has been exposed to or is at risk for exposure to Bacillus anthracis, Yersinia pestis,
  15 Variola major, Histoplasma capsulatum, Haemophilus influenzae, Escherichia coli, Shigella flexneri, S. dysenteriae (Shigella bacillus), Salmonella, Staphylococcus enterotoxin B, Ebola virus, tick-borne encephalitis virus, botulinum toxin, ricin toxin, cobra venom, shellfish toxin, botulinum toxin, saxitoxin, ricin toxin, tricothecene mycotoxin, or aflatoxin, comprising administering to the subject a
  20 therapeutically effective amount of an immunostimulatory D oligodeoxynucleotide or an immunostimulatory K oligodeoxynucleotide and an anti-infective agent, thereby treating or preventing the infection.
- 19. The method of claim 18, wherein the anti-infective agent is an antibiotic, an antiviral compound, an anti-fungal compound, or hyper-immune globulin.
  - 20. The method of claim 18, wherein the subject has been exposed to or is at risk for exposure to *Bacillus anthracis*.
- 30 21. The method of claim 18, wherein the subject has been exposed to or is at risk for exposure to Ebola virus.

- 22. The method of claim 18, wherein the subject has been exposed to or is at risk for exposure to tick-borne encephalitis virus.
- 23. The method of claim 18, wherein the infection is anthrax, smallpox,Ebola, or tick-borne encephalitis.
  - 24. The method of claim 23, wherein the infection is anthrax.
- 25. The method of claim 25, wherein the oligodeoxynucleotide is at least about 16 nucleotides in length and comprises a sequence represented by the
   following formula:

5' X<sub>1</sub>X<sub>2</sub>X<sub>3</sub> Pu<sub>1</sub> Py<sub>2</sub> CpG Pu<sub>3</sub> Py<sub>4</sub> X<sub>4</sub>X<sub>5</sub>X<sub>6</sub>(W)<sub>M</sub> (G)<sub>N</sub>-3'

wherein the central CpG motif is unmethylated, Pu is a purine nucleotide, Py is a pyrimidine nucleotide, X and W are any nucleotide, M is any integer from 0 to 10, and N is any integer from 4 to 10.

15

- 26. The method of claim 25, wherein N is about 6.
- 27. The method of claim 25, wherein Pu<sub>1</sub> Py<sub>2</sub> CpG Pu<sub>3</sub> Py<sub>4</sub> are phosphodiester bases.

20

- 28. The method of claim 25, wherein  $X_4X_5X_6(W)_M(G)_N$  comprises one or more phosphothicate bases.
- 29. The method of claim 7, wherein  $X_1X_2X_3$  Pu Py and Pu Py  $X_4X_5X_6$  are self-complementary.
  - 30. The method of claim 18, wherein the oligodeoxynucleotide comprises a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ

63

ID NO: 18, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, and SEQ ID NO: 25.

31. The method of claim 18, wherein the oligodeoxynucleotide comprises a sequence represented by the following formula:

5' N<sub>1</sub>N<sub>2</sub>N<sub>3</sub>Q-CpG-WN<sub>4</sub>N<sub>5</sub>N<sub>6</sub> 3'

wherein the central CpG motif is unmethylated, Q is T, G or A, W is A or T, and  $N_1$ ,  $N_2$ ,  $N_3$ ,  $N_4$ ,  $N_5$ , and  $N_6$  are any nucleotides.

32. The method of claim 31, wherein Q is a T.

10

15

5

- 33. The method of claim 18, wherein the oligodeoxynucleotide comprises a sequence selected from the group consisting of SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, and SEQ ID NO: 43.
- 34. The method of claim 18, wherein the oligodeoxynucleotide is administered intravenously, intra-muscularly, subcutaneously, or by inhalation.
- 35. A method of treating or preventing an infection in a subject who has been exposed to or is at risk for exposure to *Bacillus anthracis*, comprising administering to the subject a therapeutically effective amount of an immunostimulatory D oligodeoxynucleotide and an anti-infective agent,

wherein the oligodeoxynucleotide is at least about 16 nucleotides in length and comprises a sequence represented by the following formula:

5' X<sub>1</sub>X<sub>2</sub>X<sub>3</sub> Pu<sub>1</sub> Py<sub>2</sub> CpG Pu<sub>3</sub> Py<sub>4</sub> X<sub>4</sub>X<sub>5</sub>X<sub>6</sub>(W)<sub>M</sub> (G)<sub>N</sub>-3'

wherein the central CpG motif is unmethylated, Pu is a purine nucleotide, Py is a pyrimidine nucleotide, X and W are any nucleotide, M is any integer from 0 to 10, and N is any integer from 4 to 10, thereby treating or preventing the infection.

64

36. A method of treating or preventing an infection in a subject who has been exposed to or is at risk for exposure to *Bacillus anthracis*, comprising administering to the subject a therapeutically effective amount of an immunostimulatory K oligodeoxynucleotide and an anti-infective agent,

wherein the oligodeoxynucleotide comprises a sequence represented by the following formula:

wherein Q is a T, and

wherein the anti-infective agent is hyper-immune globulin.

10

5

- 37. A method of enhancing the immunogenicity of a vaccine against a bioterrorism agent in a subject, comprising administering to the subject a therapeutically effective amount of an immunostimulatory D oligodeoxynucleotide or an immunostimulatory K oligodeoxynucleotide in combination with the vaccine, thereby enhancing the immunogenicity of the vaccine.
- 38. The method of claim 37, wherein the vaccine is an antigen vaccine, a DNA vaccine, a protein subunit vaccine, a peptide vaccine, an attenuated vaccine, or a heat-killed vaccine.

20

25

30

- 39. The method of claim 37, wherein the vaccine is a vaccine against Bacillus anthracis, Yersinia pestis, Variola major, Ebola virus, tick-borne encephalitis virus (TBEV), Histoplasma capsulatum, Haemophilus influenzae, Escherichia coli, Shigella flexneri, S. dysenteriae (Shigella bacillus), Salmonella, or Staphylococcus.
- 40. The method of claim 37, wherein the vaccine is an antigen from *Bacillus* anthracis.
- 41. The method of claim 40, wherein the antigen is recombinant Protective Antigen or Protective Antiogen.

65

- 42. The method of claim 37, wherein the vaccine is Anthrax Vaccine Attenuated.
- 43. The method of claim 37, wherein the oligodeoxynucleotide is at least about 16 nucleotides in length and comprises a sequence represented by the following formula:

5' X<sub>1</sub>X<sub>2</sub>X<sub>3</sub> Pu<sub>1</sub> Py<sub>2</sub> CpG Pu<sub>3</sub> Py<sub>4</sub> X<sub>4</sub>X<sub>5</sub>X<sub>6</sub>(W)<sub>M</sub> (G)<sub>N</sub>-3'

wherein the central CpG motif is unmethylated, Pu is a purine nucleotide, Py is a pyrimidine nucleotide, X and W are any nucleotide, M is any integer from 0 to 10, and N is any integer from 4 to 10.

10

5

- 44. The method of claim 43, wherein N is about 6.
- 45. The method of claim 43, wherein Pu<sub>1</sub> Py<sub>2</sub> CpG Pu<sub>3</sub> Py<sub>4</sub> are phosphodiester bases.

15

46. The method of claim 43, wherein  $X_4X_5X_6(W)_M(G)_N$  comprises one or more phosphothioate bases.

4.

25

- 47. The method of claim 43, wherein X<sub>1</sub>X<sub>2</sub>X<sub>3</sub> Pu Py and Pu Py X<sub>4</sub>X<sub>5</sub>X<sub>6</sub> are self-complementary.
  - 48. The method of claim 37, wherein the oligodeoxynucleotide comprises a sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, and SEQ ID NO: 25.
  - 49. The method of claim 37, wherein the oligodeoxynucleotide comprises a sequence represented by the following formula:

66

## 5' N<sub>1</sub>N<sub>2</sub>N<sub>3</sub>Q-CpG-WN<sub>4</sub>N<sub>5</sub>N<sub>6</sub> 3'

wherein the central CpG motif is unmethylated, Q is T, G or A, W is A or T, and  $N_1$ ,  $N_2$ ,  $N_3$ ,  $N_4$ ,  $N_5$ , and  $N_6$  are any nucleotides.

- 50. The method of claim 13, wherein Q is a T.
  - 51. The method of claim 37, wherein the oligodeoxynucleotide comprises a sequence selected from the group consisting of SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, and SEQ ID NO: 43.
  - 52. The method of claim 37, wherein the oligodeoxynucleotide is administered before the vaccine is administered to the subject.

15

20

10

- 53. The method of claim 52, wherein the oligodeoxynucleotide is administered from about two weeks to about one day before the vaccine is administered to the subject.
- 54. The method of claim 37, wherein the oligodeoxynucleotide is administered to the subject concurrently with the vaccine.
  - 55. The method of claim 37, wherein the oligodeoxynucleotide is administered after the vaccine is administered to the subject.

- 56. The method of claim 55, wherein the oligodeoxynucleotide is administered from about two weeks to about one day after the vaccine is administered to the subject.
- 57. A method of enhancing the immunogenicity of an anthrax vaccine, comprising administering to the subject a therapeutically effective amount of an

67

immunostimulatory D or K oligodeoxynucleotide and an anthrax vaccine, thereby enhancing the immunogenicity of the vaccine.

58. The method of claim 59, wherein the vaccine is Protective Antigen.

5

59. The method of claim 59, wherein the vaccine is Anthrax Vaccine Attenuated.